been in some of these patients the treatment of choice. In fact, it has to be considered as the gold standard. Additionally, according to a recently published, well conducted systemic review 5-year survival rate (including perioperative mortality of up to 5%) after resection for HCC fulfilling MC was 67% (27–81%) [5].

Otto *et al.* [1] report a similar overall 5-year survival rate of 70% following transplantation, but it remains unclear why resection was not attempted at least in selected patients in the presented series.

Furthermore, liver transplantation seems to offer a very limited 5-year survival benefit in patients with Child-Pugh A liver cirrhosis when compared with resection (2.8 [4.4–57] months) or radio frequency ablation (RFA) ± TACE (5.7 [0.7–11.4] months) [6].

Moreover, TACE alone is nowadays no longer regarded as the best therapy for inoperable HCC. Combination with radiofrequency ablation, laser induced thermotherapy, selective internal radiotherapy (SIRT) or transarterial radioembolisation (TARE) can be more effective and can control the tumour in up to 70% of cases [7].

We therefore think that the data provided by Otto *et al.* [1] is

transplantation. In fact, due to multiple biases there is no evidence provided to support this conclusion of the paper.

Conflict of interest

The authors declared that they do not have anything to disclose regarding funding or conflict of interest with respect to this manuscript.

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Reply to: "How to decide about liver transplantation in patients with hepatocellular carcinoma: Size and number of lesions or response to TACE?"

To the Editor:

We appreciate the interest of A. Paul *et al.* in our recent publication "How to decide about liver transplantation in patients with hepatocellular carcinoma: Size and number of lesions or response to TACE?" [1]. The point in this publication was to demonstrate the vagueness of size and number of HCC nodules in initial imaging to predict tumour recurrence when compared to the results of pretransplant transarterial chemoembolization (TACE). Based on a cohort of 136 patients uniformly treated by repeated TACE, the results of the radiological routine assessment before the first TACE and after the last TACE before liver transplantation (LT) were compared. Carcinomas remaining stable or responding to TACE during pretreatment had a favourable prognosis. Their reduced recurrence rate – when compared with tumours with progression during TACE – does clearly reflect favourable tumour biology, and the pre-treatment used in our cohort was obviously capable of separating two biologically different groups of patients. The question remains if response to TACE is really a surrogate of tumour biology or if proof of time is crucial in biological selection. If time before LT is crucial any other form of pre-treatment would yield similar results. Nothing more – but also nothing less – is claimed in our publication. We cannot see the "confusion" in this statement.

Most other aspects criticised by the authors of the letter go beyond the scope of our publication. This applies for issues such as drop-out rate including the rate of patients functionally

deteriorating during TACE [2], comparison of LT with liver resection and with forms of HCC treatment such as radiofrequency ablation, TACE using drug eluting beads, ^{90}Yttrium therapy, etc. We agree that liver resection may offer a similar survival benefit as LT. That is particularly true for Asian countries, less for the Western world [3]. This differential indication was, however, not the point of our publication. Likewise, the problem if lab-MELD, matchMELD, regular or rescue allocation impact prognosis was not intended to be addressed, as it deserves studies using a much greater cohort of patients and can, therefore, not be answered by a single centre analysis. Even if described in the publication we would stress the following aspects mentioned by the authors of the letter: TNM classification usually indicates pTNM and has, therefore, to be deduced from the surgical specimen (Table 2, [1]) not being available during the initial assessment. Considerations about the indication for LT in patients with T1 or T2 tumours are justified in scientific context but must be questioned in clinical practise due to the impreciseness of imaging (29 of 70 = 41%; [4]). Of course, all patients were included in the overall survival analysis and time from first TACE to LT – the only period which is of interest in the study context – is demonstrated in Table 1, [1]. After all, we cannot recognize the "bias" challenged in the Letter as the authors ignore the issue of our publication.

In one point we agree explicitly with the authors of the submitted letter: A change of the allocation rules based on our publication would be premature and the "...finding(s) should be verified in a larger prospective study..." as stated in the last sentence of the publication.

Conflict of interest

The author declared that he does not have anything to disclose regarding funding or conflict of interest with respect to this manuscript.

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Coordinated care in cirrhosis; the need for further randomized controlled trials

To the Editor:

We read with interest the recent study on care coordination for cirrhotic patients by Morando *et al.*, with an accompanying editorial [1,2]. Firstly, we would like to congratulate the Padova group for focusing their research interest on this important topic and patient population.

We must, however, correct the statement of the editorialists that this study represents the "first prospective trial in the cirrhosis population" [2]. We highlight the publication of our own randomized controlled trial of coordinated cirrhosis care, which preceded the publication of the Padova study in the literature [3].

Referencing of our earlier study may have been helpful for the readership because, unlike the Padova study, it was a fully randomized controlled trial (RCT) with outcomes that were very different. We did not detect any improvement in either hospitalization measures or mortality in the 12 months following an intervention with a care co-ordination model.

A major limitation of the Padova study is its lack of a blinded and completely randomized group allocation procedure, which was instead based on retrospective matching of known confounders. As a consequence, it remains possible that the beneficial effects seen were not related to the new care model, but instead to more competent physicians in the intervention team or to unknown confounders that were not balanced between the groups. Unfortunately details of the allocation procedures provided are insufficient to determine the levels of stratification used for each confounder and whether all patients commenced their treatment programs within a similar timeframe following discharge.

There was also a lack of process measures performed during the trial, which would help support claims that the model was effective. For example, there were no data confirming that preventative medications prescribed were actually taken by patients, or that patient attendance at scheduled appointments was improved. Authors propose increased contacts with specialist physicians as explanation for improved outcomes in the coordinated care group. However, no analysis was performed to support the claims for associations between outcomes and greater specialist visit numbers being associated with reduced risk of mortality.

In relation to mortality, the authors chose not to discuss the distribution of events throughout the study. A careful examination of the Kaplan Meier curves does however reveal some important details. Firstly, there was an increased risk of death for standard care patients during the first 3 months of the trial relative to